

1893

M Y X O E D E M A  
AND  
S P O R A D I C C R E T I N I S M  
WITH SPECIAL REFERENCE TO  
THEIR TREATMENT  
WITH THYROID JUICE.

BY

H. GREVILLE HUIE, M.B; C.M. 1893.

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## INTRODUCTION.

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There is a most seductive charm about the unknown and I think all must confess that in Medicine as in all other sciences those subjects which are most imperfectly understood have the greatest charm for us. If all were become known - and if such a thing were possible, - all science had become exact the poor unemployed scientist having like Alexander "no more worlds to conquer" would probably die of ennui. There has thus always been, to my mind, a delightful halo of mystery around the whole subject of the Thyroid body and its functions and that curious train of diseases connected with it which have been lately the subject of so much speculation and observation and about which, until recent times, so little has been really known. What had been brought to light, however, had been of such a nature as to suggest the likelihood of discoveries of extraordinary interest in the immediate future. It seemed therefore to me quite in accordance with the order of things when, at the annual meeting of the British Medical Association at Bournemouth in July 1891,<sup>(1)</sup> a paper was read by Dr George Murray of Newcastle-on-Tyne on the successful treatment of

(1). *British Medical Journal* Aug. 8<sup>th</sup> 1891.

" " " Oct. 10<sup>th</sup> 1891.

Myxoedema by the exhibition of Thyroid juice.

This is the age of discovery; but seldom do we hear of one so complete and satisfactory, in its first blush, as this, or so likely to open up the way to other discoveries not only in the region of therapeutics but also of physiology and pathology.

Of course its great and direct interest for suffering humanity will be seen to be in its practical utility as a cure, - than which we cannot think of one more ready and certain, - for numbers of poor creatures who up till now have been always gravely assured that hope of cure might be put aside and that they might make up their minds to bear their weighty burdens to the grave, with only the possibility of amelioration of their sufferings in most cases ridiculously slight in comparison with the untiring perseverance required for carrying out the means. But the interest in this discovery to the pathologist and physiologist is also very great for as I will show hereafter, it confirms in the most decisive manner the conclusions arrived at by Professor Victor Horsley<sup>(1)</sup> and others who have, step by step, in the course of recent researches,<sup>(2)</sup> been to a great extent clearing away the cloud of mystery which has always hung around the whole subject, and as will be seen it even brings us a step nearer the

(1) Brown lectures (1884) - British Medical Journal Jan 17 & 31. 1885.  
also British Medical Journal Jan. 30 & Feb. 6. 1892.

(2) Report of Myxoedema Committee of Clinical Soc. of London. 1888. &c



solution of the question of the exact function of the Thyroid body.

### Historical Sketch.

It is essential I think to preface an account of the disease itself by a sketch of the history<sup>(1)</sup> of Myxoedema or rather of what has been said and written about it from its first debut as an individual disease or "clinical entity" among the "ills that flesh is heir to;" but that history is a surprisingly limited one, going back only twenty years. No one who has once seen a case of Myxoedema, in any degree presenting the typical features of the disease, and who has remarked the very distinct chain of symptoms and clearly defined signs which characterise it, can help wondering how it was never publicly described as a separate disease till so short a time ago and how the older physicians could have omitted to remark its individuality. They seemed, however, in these "good old days" to be content with wider definitions and fewer distinctions among diseases than will satisfy us in this age of accuracy. Thus typhus and typhoid fevers were considered varieties of the same complaint till Jenner pointed out what to us seem very apparent differences. In the same way it seems that Myxoedema was looked upon as a form of Bright's disease.

(1) Many facts in this sketch are derived from the Clinical Soc<sup>y</sup> Report, from Dr. Brauer's "Atlas of Clinical Medicine" etc.



However; though it was not until the year 1873 that Myxoedema was first publicly described, it is certain that some at least had long before this noted it as an "undescribed disease." Dr Ord himself, whose name will always take the leading place among the exponents of the disease and all connected with it, had made observations on it as far back as 1861.<sup>(1)</sup> Sir Andrew Clark has said that in 1870 he "had been familiar with the class of cases so well described by Ord under the name of Myxoedema" and had collected many facts with reference to that disease, and again Dr Byrom Bramwell tells how his<sup>(2)</sup> father, whom he joined in practice in 1869, then showed him a typical case of the disease, pointing out to him all its essential features, - "the peculiar character of the oedema, the normal condition of the urine, the character of the skin of the face and eyelids, the dulness of the intellect, the remarkable slowness of thought and speech, the persistent low temperature and the fact that the patient was extremely susceptible to cold."

Though we thus see that the disease had been individualised by some private observers, we cannot tell how long ago; it was not until 1873 that it was publicly described by Sir William Gull in a paper read before the Clinical Society of London,<sup>(3)</sup> the society which, I think I may safely say, has done

(1) *Clinical Society Report*

(3) *Transactions* Vol. vii. p. 180.

(2) *D. B. "Atlas".*

almost everything, until recently, towards the elucidation of all that has to do with Myxoedema. Sir William Gull did not give this newly defined condition a name; but called it "a cretinoid state supervening in adult life in women." It is clear from the use of this term that he considered Myxoedema to have intimate resemblances to cretinism, the sporadic form of which condition is considered by most investigators of the present time to be actually the infantile form of Myxoedema. He not only associated the disease with cretinism in this way; but he thought the causation of Myxoedema might be connected with disease or atrophy of the Thyroid gland, which for hundreds of years had been vaguely associated with the causation of cretinism.

Dr Ord was the first to apply the name Myxoedema to the disease described by Gull, and in 1877, in a communication made to the Royal Medical and Chirurgical Society of London,<sup>(1)</sup> he gave the results of observations dating as far back as 1861. This name was chosen from the fact that in the autopsy of one of his cases mucin was found in large quantities in the sub-cutaneous tissues, and he considered this to be the most characteristic symptom of the disease.

Dr Ord did not confine his observations to the clinical aspects of the matter; but went into the

(1) Transactions vol. lxi. p. 71

pathological also, and his paper contained observations on the state of the Thyroid gland in Myxoedema and he stated that it was either atrophied or changed into fibrous tissue. Ord, like Gull, considered it to be a disease confined to women; but as soon as cases of it were recognised all over the kingdom, it was found that men also were liable to becoming Myxoedematous.

In 1881 Charcot,<sup>(1)</sup> who, it seems had also been making observations for a long time, published his results, giving to the disease the name of "cachexie pachydermique."

In 1882 a Swiss surgeon, Reverdin,<sup>(2)</sup> published the results of a number of cases of total thyroidectomy in goitrous patients, and pointed out that a remarkable series of symptoms generally were found to follow this operation, and in the following year the relation of these symptoms with Myxoedema was remarked by the same observer.

Kocher,<sup>(3)</sup> however, made similar but independent observations and described the series of symptoms following total extirpation of the Thyroid gland under the name of "cachexia strumipriva." He did not consider these symptoms to be the result of loss of function of the Thyroid gland; but to be due to a condition of chronic asphyxia due to operative

<sup>1</sup>  
<sup>2</sup>  
<sup>3</sup> } Clin. Soc. Report.



interference with the structure of the neck.

It was these observations of Kocher's which led Dr Felix Seman<sup>(1)</sup> to bring the matter before the Clinical Society of London and to conclude that the loss of function of the Thyroid gland was a condition common to Myxoedema, cachexia strumipriva and cretinism, and probably the cause of all alike.

The Clinical Society then appointed in December 1883 a committee to consider the whole subject of Myxoedema and its allied conditions, and among the valuable work done by that committee perhaps the most valuable of all was Mr Horsley's experiments on monkeys, by which he succeeded in demonstrating that loss of function of the Thyroid produces in these animals "all the symptoms known as Myxoedema and cachexia strumipriva and that the condition called sporadic cretinism was but a more chronic form of these conditions.

#### Clinical Picture of Myxoedema.

The clinical picture presented by a well-marked case of Myxoedema is such that there can be little difficulty in recognising the disease at once. It has been remarked that there is a striking personal likeness between all cases. However unlike they have been at one time, as the disease advances they

(1) Clin. Soc's Report.

all get to resemble each other closely like the members of one family.

The physiognomy has only to be noted once to be always remembered: - The shapeless unwieldy figure and obvious swelling of the whole body, the "square" face and "spade-like" hands, the peculiar yellowish waxy tint of the skin with the bright pink or purple colouring of the malar region and nose, the eyes almost closed and with baggy swellings beneath the lower eyelids, the upward wrinkling of the forehead by contraction of corrugated<sup>or</sup> ~~ed~~ supercillii, the scanty hair and absence of eyebrows and eyelashes, the slow ungainly movements and awkward gait, the "leathery" voice and general air of "lethargic good temper." Such is the clinical picture; but on closer examination of almost every case we get a great number of symptoms which are practically always present, and I propose devoting the next few pages to a critical analysis of the symptoms and other particulars of the disease. In doing so, I will follow as closely as convenient the order in which they are given in the Report of the Committee of the Clinical Society of London, mentioned above, - giving, however, as much as possible my own experiences regarding each detail; but where this is wanting, giving the conclusions furnished by the Report, or information

derived from other sources. I may mention here that my personal experience of Myxoedema is limited to several cases which I saw in hospital as a student, <sup>about</sup> a dozen cases which I have seen at present under treatment by doctors in Edinburgh, and one which I have had the good fortune to have under my own care for the last three months. The particulars of some of these I propose to give more or less fully hereafter and my own case will be given at length, with the results of treatment by "Thyroid feeding."

#### Analysis of Symptoms of Myxoedema: Age.

Age: All the cases I have seen have been between 30 and 60; but cases have been known so young as <sup>8</sup>13 and 20. Myxoedema and sporadic cretinism have been so long considered to be different diseases that it is quite necessary to consider them individually and the following notes refer to the former alone. As I have had considerably less experience of sporadic cretinism than of Myxoedema, I shall only give a comparatively brief notice of its features and details and shall devote a later part of this paper to that purpose. If we think of sporadic cretinism as the same disease as Myxoedema, which in reality it is, having most of the features of the latter plus all the features of arrested development, then we get it of course congenital. There are other rare



cases of sporadic cretinism, however, in which the disease has commenced some years after birth - Dr Hilton Fagge in his classical paper in 1871 tells of a case which commenced at 8 years of age, and in the British Medical Journal for 20th January 188<sup>3</sup>, a case is mentioned by Dr Coxwell commencing at the same age.<sup>(1)</sup>

To my mind these latter cases appear as a link between the two conditions - there not being a very wide gap between these cases and early cases of Myxoedema.

### Sex.

I have seen it in both sexes, but in many more women than men. Sir William Gull originally described it as "supervening in adult life in women," and Dr Ord also for a long time considered it to be a disease of women only. Sir Andrew Clark has stated that in his experience it appears in the proportion of seven cases in males to three in females.<sup>(2)</sup> The Clinical Society's Report gives one in males to six in females.

### Social Conditions.

It occurs alike in all grades of society.

(1) This case at the time was considered to be one of Myxoedema

(2) Ord's Art. Myxoedema in Quain's dictionary of medicine - foot note.

At meeting of Clinical Society of London Nov. 8. 1889 Dr. Abernethy mentioned a case of his of Myxoedema, which had developed the disease at the age of 8 or 9 years - See British Medical Journal - Nov. 16. 1889.

### Family Antecedents.

I have seen it in twin sisters, patients of Dr Melville Dunlop's, and there is no doubt that their mother and a third sister were sufferers from Myxoedema.

### Personal Antecedents. Aetiology and Mode of Onset.

The Clinical Society's Report mentions that mental disturbance has sometimes a determining effect. In several of the cases which I have met with there was a very distinct history of great worry or mental strain, before the commencement of symptoms. Again, at the meeting of the Edinburgh Medico-Chirurgical Society on February 15th and 16th 1893, at which Myxoedema and its treatment by Thyroid juice were fully discussed, and at which I was present, Dr Affleck remarked<sup>(1)</sup> that he thought it was of importance to inquire into the antecedents, as in most of his cases, and he had had many, there had been a history of antecedent depressing influence, such as worry and anxiety, consequently that the underlying nervous influence should not be lightly put aside. He had found insanity not infrequent as a termination, but one case was remarkable in that the order of affection was reversed, the patient suffering first from cerebral haemorrhage followed by hemiplegia, then

(1) Report of this meeting in the "Medical Week": Feb. 24. 1893.

from cerebral softening with insanity, and lastly from Myxoedema." Many cases seem to date from a severe labour.

One case I have seen, also a case of Dr Melville Dunlop's, appeared to commence with the disappearance of goitre under treatment and atrophy of the Thyroid. Alcoholism and syphilis have not their usual prominence as causes of this disease at least.

Myxoedema is a slowly developing disease, coming on insidiously, and is often not noticed for months after it has commenced, the patient only experiencing increasing listlessness and disinclination for exertion of all sorts; then perhaps the alteration in speech is noticed by friends and in course of time the swelling becomes apparent. But not infrequently one hears of the disease commencing very rapidly, and this is well explained by Dr Byrom Bramwell in his new "Atlas of Clinical Medicine," where he says "It is, I think, probable that in most if not all of the cases of Myxoedema in which the symptoms are said to develop rapidly, the disease has for some time been in existence unknown to the patient. It is a common and every-day experience to find a disease which has been slowly and insidiously developing unknown to the patient, suddenly aroused,



as it were into activity by some intercurrent acute affection, or indeed by some comparatively trifling and temporary disturbance of the general health.

The date at which the symptoms are first perceived by the patient is in many cases a very fallacious guide to the actual date of onset. The patient naturally dates the onset of the disease from the time at which he first became conscious of its presence, i.e., from the time at which the symptoms were first noticed."

#### Catamenia.

This, in most of the cases I have seen, has been in abeyance; but such is not universal. In the case which I have had under treatment (and which for convenience I will hereafter refer to as the case of A.B.) menstruation had gone on regularly till six months before treatment was begun.

At a meeting of the Harveian Society of London on 20th October 1887,<sup>(1)</sup> Dr. M.H. Jones remarked that long and severe menorrhagia was a most prominent symptom in several cases of Myxoedema he had observed.

#### Pregnancies and Children.

Many cases of Myxoedema, as mentioned above, seem to date from the time of a confinement as in

(1) *British Medical Journal*. Nov. 5. 1887.

the case of A.B. As a rule pregnancy does not seem to occur during the course of the disease, but in the Clinical Society Report it is said that "It is certain that Myxoedema is no bar to pregnancy and furthermore that gestation may occur and go on to its full period in the advanced stage of the disease"

#### Symptoms. Bulk and Weight.

This has been much increased in all cases I have had experience of, and, as will afterwards be seen, the extraordinary loss of weight which is a universal and most striking result of the treatment by Thyroid juice, is an indication of the corresponding increase which had occurred during the course of the disease. At the meeting of the Edinburgh Medico-Chirurgical Society mentioned above, Dr W. Russell showed a patient whose weight was 22 stones.

#### Physiognomy.

The point that strikes <sup>me</sup> most about the physiognomy of these patients is the want of expression in the face, - the oedema seems to "wipe out" all signs of this. In fact, one can form a good idea of the gravity of a case by noting the amount of expression that remains, if any.



This photograph, of a patient of Dr. Dunlap's, taken at the commencement of treatment, shows very well many of the characteristic features in the physiognomy of myxædema. The eyelids were so swollen in this case that the patient had to open her eyes with her fingers before she could see.



Face.

The colour of the skin generally is a tawny yellow with a waxy transparency which reminds me of the faces of these little images of their gods which the Chinese hang about their persons. There is often a bright pink or purple patch on each malar region and on the nose somewhat in the form taken by a certain description of lupus of the face which Dr Jamieson calls "butterfly lupus." The form of the face is much distorted, getting a broadened, square, coarse look. The eyelids are puffy and swollen, and there is a baggy swelling under the lower eyelids. The closure of the eyes causes a compensatory contraction of the corrugator supercilii. In a case of Dr Melville Dunlop's ( the photograph of which I have affixed opposite) the eyes were so closed up that the patient had to hold them open with the fingers before she could see out of them. The nose is flattened out, and the lips are thick and coarse, the under lip hanging down and everted in a characteristic manner. The tongue is often too large for the mouth and sometimes protrudes. In one of Gull's original cases, the tongue was so large that false teeth could not be worn. The condition of the tongue also gives rise to the "leathery" tone of the voice. The mucous membrane

of the mouth is swollen. The soft palate is swollen also and causes snoring.- the larynx also. A copious mucous discharge from the mouth is not uncommon. A.B. was much annoyed by this discharge which used to pour out of her mouth at night and soak the pillow.

### Skin.

There is generally marked absence of perspiration and sebaceous secretion - the skin becomes hard, dry and scaly. On the scalp thick dark-coloured crusts form, which are with difficulty removed. Brown patches of pigmentation are not uncommon, and flat warts are common on different parts of the body. Late in the advance of the disease "patches of dilated vessels, purpuric patches and ecchymoses" in various positions are found at times. Fatty swellings are a very characteristic feature and are exceedingly common in the supra-clavicular region, second in frequency in front of the axilla and less often found between the shoulders.

### Hair, Nails and Teeth.

There is a great tendency for the hair to fall out and in many cases almost complete baldness is present; but what hair remains is ragged, dry and coarse. The eyebrows and eyelashes are markedly

absent, but curiously enough, when the subjects of the disease are males, the beard and moustache do not show the same tendency to fall out.<sup>(1)</sup>

The nails become brittle and get cracked and split, and the teeth likewise chip and crack and quickly decay.

#### Extremities.

The hands are broadened and "spade-like" and the feet similarly affected.

#### Abdomen.

It is specially prominent and umbilical hernia may occur; this, however, is much more common in sporadic cretinism.

#### Muscles, etc.

The muscles feel to the patient as if "bound" and difficult to work. To objective examinations they feel hard and board-like - those of the back of the neck sometimes remarkably so.

#### The solid Oedema.

This is always present over the body generally and is solid and elastic and does not pit on pressure. Professor Greenfield pointed out, at the meeting of the Edinburgh Medico-Chirurgical Society

(1) Professor Greenfield - meeting of Edinb. Medico-Chir. Soc. 15. Feb.



mentioned above, "that the oedema appears to owe its characters to the fact that it is deeply situated, the changes being in the sub-cutaneous tissue."

#### Presence of Watery Dropsy.

This is fairly common; but it is exceptional to have it as a persistent symptom.

#### Temperature.

Practically universally sub-normal - i.e. 94° F. to 97° F. or so.

#### Condition of Thyroid Body.

The Thyroid cannot be felt as a rule, though this is no satisfactory indication of its atrophy, as the oedema of the neck would obscure even a normal gland. In a case which has already been mentioned, the Thyroid had been enlarged so that the case was looked upon as one of goitre; but under treatment this enlargement disappeared and Myxoedema set in. During an engagement with the Thibetian army in 1888, a prisoner was taken who had all the characteristic signs of Myxoedema; but a Thyroid gland "so large that it extended from the lower maxilla to about one inch under the sternum" was present. He died and on post-mortem examination as far as could be made out this swelling was composed of

(1) *British Medical Journal* - April 4. 1891.

fibrous tissue in place of proper Thyroid structure. The following curious case was published in the British Medical Journal for January 7th 1893 by Dr J.G.G.Corkhill, of Birkdale. A lady, aged 32, after prolonged over-taxing of the nervous system became rapidly very listless and easily fatigued - grew pale and her legs swelled, and in two days a sensation of tightness came on in the throat and a large swelling soon appeared in the region of the Thyroid. This swelling, which was in reality a greatly enlarged Thyroid, developed in 48 hours. It appeared to be entirely vascular. A bruit could be heard all over its surface and when the patient was worried or excited it became temporarily increased in size. The swelling of the body continued, and the signs of Myxoedema developed until in September she presented all the characteristic signs of the disease. She was subjected to treatment by injection of Thyroid extract, and the enlarged gland was painted with Liniment Iodi; and in two months she was practically cured of the symptoms of Myxoedema, the Thyroid gland being reduced to about half its previous size.

When it can be made out that the gland is really diminished, it is found that the right side is more so than the left, just as in Grave's disease the right is more enlarged than the left.

Sensation.

Cutaneous sensation is retarded as might be expected.

Paresis.

This is very common, especially in the muscles of the limbs and neck.

Co-ordination.

This is greatly impaired, as is seen in the staggering gait, etc.

Retardation of Movement.

Retardation is universal, and is noticed in all movements and in the gait.

Speech.

Is slow, "leathery," often hesitating and unmelodious.

Deafness.

Deafness is rather a common symptom - possibly due to swelling of the mucous membrane round the mouth of the Eustachian tube and choking of this, and hence indrawn tympanum, etc.



### Smell and Taste.

Dr Ord mentions that "two affections of the special senses apparently related with changes of the periphery are often noticed. One a persistent unpleasant taste, something of bitterness, sometimes of sweetness, etc.; the other a persistent unpleasant smell." (1)

### Subjective Sensations.

Patients invariably complain of feeling cold, and are always in best health in warm weather. Headaches are common, and in a large number of cases aching pains are complained of in the limbs, back, etc.

### Heart and Blood-vessels.

The heart is said to be weak and dilated in almost all cases of Myxoedema. The pulse is weak and slow. The superficial capillaries are often dilated in patches.

### Bowels.

The bowels have been constipated persistently in almost all cases I have seen.

### Urine.

The urine is generally diminished in quantity.

(1) Ord's Art. Myxoedema, in Quain's Dictionary of Medicine,

the urea below normal, and specific gravity always low.

### Temperament.

Ord remarks on the "lethargic good temper," but often this alternates with irritability.

I have been much struck with the callousness and indifference which myxoedematous patients exhibit as to the future progress of their trouble, and when <sup>practical</sup> cure is actually promised to them within three or four months, they seem rather to desire only to be left alone, and are generally unwilling to submit to treatment.

### Intellectual Changes.

In practically all cases of Myxoedema there are marked intellectual changes - varying from mere "mental torpidity, slowness of apprehension, thought and action, and loss of memory, especially for recent events" <sup>(1)</sup> to insanity of most aggravated type, and nearly a quarter of the cases could, I believe, be certified as insane. Delusions and hallucinations occur in the advanced stages in a large percentage of cases, and insanity <sup>(2)</sup> "takes the form of acute and chronic mania, dementia, or melancholia, with a morbid predominance of suspicion and self-

(1) } Clinical Societies Report.  
(2) }

accusation."

Dr Elkins of the Edinburgh Royal Asylum pointed out to me the other day a case of general paralysis of the insane, which could almost have been mistaken for Myxoedema. The "wiping out" of the expression gave the face a swollen, distorted form, and loss of co-ordination, something in the speech and the "progressive dementia"<sup>(1)</sup> and several other points produced a remarkable similarity between the two diseases.

Dr Elkins has also remarked to me on the peculiar nature of the delusions which are present in one of two highly interesting cases which he has had under the "Thyroid treatment," and on which, through his kindness, I have been enabled to make careful observations during the whole course of treatment, which I give in detail later on. It has frequently been remarked that Myxoedema bears a special relation to the sexual functions, and though I had thought that no proof of any such relation had lately been brought forward, Dr Elkins is of opinion that some such cause tends to produce the extraordinary delusions of a sexual nature which this patient had, and which I understand are remarkably common in the insanity of Myxoedema.

(1) This point is also remarked by Whitwell - British Med. Journal Feb 27. 1892.



Progress and Termination of the Disease.

As has been mentioned above, Myxoedema is an extremely chronic disease and runs a protracted course of many years duration - most cases going from bad to worse until ended by some intercurrent disease, such as pneumonia, bronchitis, renal disease, etc., or some condition directly or indirectly the result of the disease, as exhaustion, coma, suffocation, etc. Some cases naturally improve to a certain extent, as did the case of A.B., and one case of spontaneous recovery is on record.

## S P O R A D I C   C R E T I N I S M.

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This condition was first described by Curling in 1850. Dr Hilton Fagge brought forward a valuable paper on the subject in 1871. Dr Byrom Bramwell in his ''Atlas of Clinical Medicine'' remarks upon the prophetic character of Dr Fagge's conclusions, which were subsequently verified and how they may be said to have paved the way for the discovery of Myxoedema, and he quotes Dr Fagge's statement as follows:-

''In the majority of cases, Sporadic Cretinism, like endemic Cretinism is congenital but case 2 appears beyond doubt to be an example of the development of the same physical state as late as the eighth year, in a child previously healthy. I believe that no instance of a similar kind has hitherto been recorded. It will be observed that in this case the peculiar physical configuration was alone manifested, or at any rate that any change in the mental powers was doubtful. It may therefore be interesting to speculate as to what characters would be present should the disease (if that were possible) arise still later

in the course of adult life. The peculiarities in the form of the cranial and facial bones, and in the bony framework generally would then probably be absent, the development of the skeleton being unalterable when once completed. And I think that we must conclude that the most marked features in such a case would be coarseness and thickness of the soft parts of the face (especially the lips), and perhaps of the subcutaneous tissues of the hands and feet, besides the presence of supraclavicular fatty tumours and possibly a wasting of the thyroid body, if that should prove to be a constant character of the disease."

It has been mentioned above that Myxoedema and Sporadic Cretinism are now considered to be one and the same disease, and indeed this was plainly the view of Dr Ord himself, the difference being that, in the latter we have the evidences of arrested development added to the ordinary signs of Myxoedema, Sporadic Cretinism commencing early in life before the bony framework is formed, and the earlier the commencement of the arrest, the more marked the cretinoid features.

Fagge considered Sporadic, to be identical with



the endemic cretinism, the chief apparent difference being the absence of the swelling above the clavicles in the latter condition. But he suggested that this is no real difference, for as these fatty swellings are diminished by ill nourishment, their absence is easily accounted for in "the small and miserable cretins of the mountains."

(1) Many causes have been suggested among the family antecedents, etc. Dr Sidney Philips, on 2nd May 1885<sup>(1)</sup> directed the attention of the Clinical Society of London to the fact that three out of the ten cases then published had a history of the mother having had a fright during pregnancy, but that in any case, as other children by the same parents were often quite healthy, the primary cause must be something which is transient and accidental.

The primary causation of the condition, has also been put down to the father having been intoxicated at the time of conception, and many other such causes are suggested.

#### Symptoms and other particulars.

The physiognomy of Sporadic Cretinism and many of the striking features are beautifully shown in a

(1) *Lancet* May. 2. 1885.

photograph illustrative of a case of this disease (p. 96) which I shall give later on, in full, when describing the effect of the 'Thyroid treatment' on it. Though in many respects suggestive of an infant only a few months old, these curious beings remind one of a little old man, and an indescribable, uncanny, look about them reminds one of the malevolent little dwarfs of German legend. The face is intensely ugly, broad and shapeless; the complexion a greyish yellow and waxy; the nose flat and snubbed, with the anterior nares perhaps pointing directly forwards; the mouth large and the lips thick, and the tongue often so swollen that it protrudes between the teeth. The supraclavicular fatty swellings are very constant and are generally well marked. In one of Fagge's cases these were 'much larger than a hen's egg' and as he states the size depends on the nutrition of the body.<sup>(1)</sup> Similar tumours may be found in front of the axilla or between the shoulders.

The head is very large and the anterior fontanelles remain open, and the cranial and facial bones are much distorted. The temporary teeth persist and are usually cracked and brittle. The head is set on a broad bull-neck. The Thyroid body is practically

(1) Fagge's Principles & Practice of Medicine Vol. I. page 879.

absent, except in one of Fagge's cases, in which the Thyroid was present but atrophied and containing a cyst. The subjects of this condition remain tiny dwarfs all their lives, and when they have attained to full adult age, are often below three feet in height. The abdomen is very prominent and an umbilical hernia is common. The hands and feet are broad and spade-like, as in Myxoedema, and the nails clubbed, ridged and brittle. The legs are often bowed, but the ends of the bones not enlarged, as in rickets. Lordosis is common.

Dr Godhart<sup>(1)</sup> mentions the irregular development of the muscles, some groups as those of the thenar and hypothenar eminences, the thighs and tongue, etc., being enlarged, while others, such as those of the calf perhaps, may be atrophied. Dr Judson Berry<sup>(2)</sup> remarks a pseudohypertrophy of the muscles. The latter observer also makes the observation that the knee jerk is increased. As in Myxoedema the skin is harsh and dry and perspiration is absent; the hair is scanty generally. The subcutaneous tissues are everywhere packed with the characteristic oedema of that condition. Dr Sidney Philips pointed out that out of the ten cases reported before 1885, namely two by Curling

(1) Medical Times & Gazette May 1st 1880.

(2) Keating's Cyclopaedia of Children's diseases.



four by Fagge, one by Fletcher Beach, one by Langton Downs and one by Routh, solid oedema was not an exceptional feature, but part and parcel of the disease, just as in Myxoedema. (1)

Often the subjects of Sporadic Cretinism can only say a few words, and the speech is slow and hesitating, and the voice harsh, cracked and unmelodious, and not at all like what one would expect from such a child-like being. All movements are slowly and awkwardly performed, and the gait waddling.

The bowels are often habitually constipated. (2)

Intellectual features.

Intellectually Sporadic Cretins differ greatly from the subjects of Myxoedema, for here we get not only dulling of the mind, but arrested development, and the amount of development of course depends upon the age at which arrest commenced. Thus we get Sporadic Cretins with considerable mental development though always the Myxoedematous dulling, as in Fagge's case, which commenced at the age of 8, and between such and those which are practically idiots, are all possible grades. Such are the features and symptoms of Sporadic Cretinism. This condition like Myxoedema

(1) *Lancet* - May, 2, 1885 - p. 799

(2) See Dr. Edward Carnichael's case in *'Lancet'* March 18, 1893

runs an exceedingly chronic course and deaths occur from intercurrent diseases usually.

PATHOLOGY OF MYXOEDEMA AND SPORADIC CRETINISM.

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Pathology.

It may be well here to consider some of the many opinions that have been formed as to the nature and causation of the symptoms of Myxoedema and Sporadic Cretinism.

It is almost universally admitted that Myxoedema and Sporadic Cretinism are due to loss of function of the Thyroid body. The results of the researches of the Clinical Society of London which appeared in their Report in 1880 seem to establish this point satisfactorily. These conclusions are as follows:- (I give here only such of the conclusions as refer to the above or kindred subjects.)

"That clinical and pathological observations, respectively indicate in a decisive way, that the one condition common to all cases is destructive change of the thyroid gland. That the most common form of destructive change of the thyroid gland consists in the substitution of a delicate fibrous tissue for the proper glandular structure.



That interstitial development of fibrous tissue is also observed very frequently in the skin and with much less frequency in the viscera; the appearances presented by this tissue being suggestive of an irritative or inflammatory process.

That pathological observation, while showing cause for the changes in the skin observed during life, for the falling off of the hair, and the loss of the teeth, for the increased bulk of the body as due to excess of subcutaneous fat, affords no explanation of the affections of speech, movement, sensation, consciousness and intellect which form a large part of the symptoms. That chemical examination of the comparatively few available cases fails to show the general existence of an excess of mucin in the tissues adequately corresponding to the amount recorded in the first observation, but that discrepancy may be in part attributed to the fact that tumefaction of the integuments, although generally characteristic of Myxoedema varies considerably throughout the course of the disease and often disappears shortly before death.

That in experiments made upon animals particularly on monkeys, symptoms resembling in a very close and remarkable way those of Myxoedema have followed com-

plete removal of the Thyroid gland performed under antiseptic precaution and with as far as could be ascertained no injury to the adjacent nerves or to the trachea.

That in such experimental cases a large excess of mucin has been found to be present in the skin, fibrous tissues and blood and salivary glands; in particular the parotid gland normally containing no mucin has presented that substance in quantities corresponding to what would ordinarily be found in the submaxillary gland.

That the full analysis of the results of the removal of the Thyroid gland in man demonstrates in an important proportion of cases the fact of the symptoms exactly corresponding with those of myxoedema being developed subsequently.

That in no inconsiderable number of cases the operation has not been known to have been followed by such symptoms; the apparent immunity being in many cases probably due to the presence and subsequent development of accessory thyroid glands, or to accidentally incomplete removal, or to insufficiently long observation of the patients after operation.

That whereas injury to the trachea, atrophy of

the trachea, injury to the recurrent laryngeal nerves and of the cervical sympathetic and endemic influences, have been by various observers supposed to be the true cause of experimental or of operative Myxoedema (cachexia strumipriva) there is, in the first place, no evidence to show that of the numerous and various surgical operations performed on the neck and throat, involving various organs and tissues, any, save those in which the thyroid gland has been removed have been followed by the symptoms under consideration; that in many of the operations on man and in most if not all of the experimental operations made by Professor Horsley on monkeys and other animals this procedure avoided all injury of surrounding parts and was perfectly aseptic; that myxoedema has followed removal of the thyroid gland in persons neither living in, nor having lived in localities the seat of endemic cretinism; that therefore the positive evidence on this point vastly outweighs the negative and that it appears strongly proved that Myxoedema is frequently produced by the removal as well as by the pathological destruction of the thyroid gland.

That a general review of symptoms and pathology leads to the belief that the disease described under



the name of Myxoedema as observed in adults is practically the same disease as that named Sporadic Cretinism when affecting children; that Myxoedema is probably identical with cachexia strumipriva and that a very close affinity exists between Myxoedema and endemic cretinism.

That while these several conditions appear, in the main, to depend on, or to be associated with the destruction or loss of the function of the thyroid gland the ultimate cause of such destruction or loss is at present not evident''.

Dr Mahomed at a meeting of the Clinical Society of London in December 1881, brought forward his conclusion in contradiction to those just quoted,<sup>(1)</sup> as to the nature and causation of Myxoedema. He suggested that all cases of Myxoedema were in reality cases of chronic Bright's Disease, and he remarked that in many cases of the latter oedema was absent, and in other cases there were all the symptoms of Myxoedema without albuminuria, but with high arterial tension. In some cases of Myxoedema the subcutaneous tissues were not found to contain excess of mucin. These cases appeared to be due to Chronic Bright's Disease without kidney symptoms as described by Sir W. Gull

<sup>(1)</sup> *Lancet* Dec. 24. 1881. etc.

and Dr Sutton. In the published cases of Myxoedema, at that time twenty in number, three were not noted as to urine. In the seventeen others ten had albuminuria, of which four were fatal and these had affected kidneys, hypertrophied hearts and thickened arteries, whilst many of the changes in the spinal cord were doubtless those of Myxoedema of the cord. Thus in all the fatal cases Bright's Disease was present. Albuminuria was absent in many cases of Bright's Disease as well as oedema.

Dr Ord, who in a Post Mortem examination on one of his cases found atrophy of kidneys and granular state of cortex, atheroma of large arteries, and thickening of arterioles, with hypertrophy of left ventricle of the heart, and effusion into the large cavities<sup>ies</sup>, expressed his belief that all these conditions might be assumed to supervene on Myxoedema.

Again in a recent number of the British Medical Journal, Mr Harry Fenwick says he believes the theory of the causation of Myxoedema is false, and that it is due to a perverted renal function and that Thyroid juice by its diuretic action removes the symptoms of the disease.

Dr Goodhart in an original communication to the

Medical Times and Gazette, May 1st 1880, gives an ingenious theory for the causation of the cerebral indolence in Myxoedema, and the undeveloped condition of the brain in cretinism. He challenges Ord's manner of accounting for those conditions which is as follows:- In Myxoedema there is a padding of new tissue round the peripheral nerves and touch corpuscles and thus being deprived of its healthy stimulation from without, the brain fails in nutrition, and more or less of mental hebitude results. The condition in Cretinism (Sporadic) is that Myxoedema being present in the infant the same sort of padding of peripheral nerves, etc, takes place, the brain is deprived thus of a large channel of education, i.e.,receptions of sensory impressions, and thus development does not proceed as in the normal condition it would.

Dr Goodhart's explanation is as follows:-

Our tissues are educated so to speak, upon a balance-of-powers principle: but if one part grows to excess, some other part will compensate by its want of development. The horticulturist adopts the principle in cultivating his plants for his special purposes; he lops here and prunes there and so forth, to make other parts of his plant grow more luxuriantly.....



If therefore the brain, the sexual organs, or any part, no matter what, which by its importance in the animal economy makes large demands upon the general stores, fails to develop properly, or is removed from taking its accustomed part in the general consumption and discharge, there is a lessened drain upon the stock, and other parts are not unlikely to gain thereby, and to become hypertrophied. In Cretinism the brain development is arrested in obedience to what conditions at first we know not, and the connective tissues hypertrophied in consequence. But here the question arises, why the connective tissue and not other tissues? For two reasons. First, it is low in the scale of development, and differentiation, and nearest to embryonic tissue, and we know that the lower the tissue, the more perfect the repair, and the lower tissues frequently hypertrophy both generally and locally, as in tumours. Secondly, connective tissue is at the fountain head of supply. Thus Dr Goodhart says the error in Sporadic Cretinism is central: the arrest of development of the brain is primary, due to unknown causes and the overgrowth of connective tissue is secondary and compensatory to this.

But he says Myxoedema is a senile degeneration affecting the intercellular connective tissues in all parts of the body. It is widely distributed through the tissues, and why should the brain and spinal cord be exempt? It is, thus a degenerative and not a small cell growth, of inflammatory nature, according to Dr Goodhart.

In a post mortem examination, however, made with reference to this question, whether the nervous system underwent any degeneration in such cases, or whether the altered sensibility, etc., were due to a mere interposition of a mucoid padding around the nerve endings, etc., and where the tissues were very carefully prepared for examination, the spinal cord was found not to be sclerosed, but a general increase of connective tissue was found in all parts. The walls of the vessels and central canal were thus affected, but no degeneration of pure nerve structure was found. Professor Greenfield, who was pathologist at St Thomas' Hospital, and examined the case of Myxoedema, from which Dr Ord first described the disease, speaking at the meeting of the Edinburgh Medico-Chirurgical Society on Feb. 15 and 16, 1893 said:- "That he thought it had been too freely assumed that there was

great deterioration of the brain. He had been struck by the great amount of intelligence that accompanied loss of consciousness of surroundings. If the cerebrum were so altered, how was the total resuscitation within a few weeks under treatment to be explained. He thought it was simply to a large extent the case of the patients' giving up the attempt to find expression in language or otherwise, because of the physiological difficulty."

In the above remarks I have not attempted to give anything like an exhaustive account of the pathology of this subject, but have merely taken up some special questions which have been of more interest to me than others; though there are many other questions equally deserving of remark which I have been obliged to leave untouched.

(1) Report of the meeting in the "Medical Week" Feb. 24. 1893



PREVIOUS TREATMENT OF MYXOEDEMA AND  
SPORADIC CRETINISM.

Previous treatment.

When, after innumerable attempts to gain some end, the long coveted goal is at last reached, through, as is often the case, some comparatively simple means it is interesting and instructive "to fight our battles o'er again", calling to mind all the struggles which only ended in failure and the efforts which, if successful at all, were rewarded only by successes insignificant in proportion to the degree of effort, remembering how gratified we were if, in a case like the present, of what was accepted as an incurable disease, we managed to get some appreciable improvement, which after all might have taken place in nature's unaided course. I propose then to glance back over the previous attempts at cure and means of treatment, not only on account of the historical interest attached to such an enquiry, but also because I think that, in the brilliant light of this newly discovered treatment, we should not lose sight of the older remedies, many of which were gained by long and untiring labour, and were really of some considerable use in relieving the symptoms at least. I quite concur with the remark made by Professor Greenfield at the meeting of the Medico-Chirurgical Society mentioned above that the older remedies should not be neglected. By keeping up the use of

these older remedies, as accessories to the new treatment and to help to make the cure more perfect and more rapid, if that be advisable, - by noting carefully the chief manner in which they acted, and perhaps finding some principle in their action common to all, we may get a clue to the manner in which this new remedy, as a drug, brings about its effects, and thus in time possibly find a clue to the physiological principle of the functions of the thyroid body.

That Thyroid juice has been proved to be a 'cure' for Myxoedema is, I think, only one of the advantages gained for medicine by this discovery. It seems to me that it has put us on the scent, which, if properly followed up, will lead to the complete elucidation of the mystery which has hung around the Thyroid and its function, and the curious diseases which seem all to be closely bound up with its fortunes.

Ord, in his article on Myxoedema in Quain's Dictionary of Medicine, says, - "Something may be done by keeping the patient carefully sheltered from cold, something by tonics, something by good food. Though these will not cure, they will at least help the patient to bear her suffering better. Of late the writer has found, in two cases, benefit from the use of vapour baths. In three others, under the prolonged use of jaborandi, the signs of Myxoedema have almost disappeared. Nitro-glycerine has benefited one case. Dr Andrew Clark regards the disease as 'partly curable by careful diet, Iron, Arsenic, baths and assiduous friction'."

Dr Ord here mentions, I think, all the chief modes of treatment that were found to be beneficial

before the introduction of the "Thyroid treatment" and certainly some cases, which were treated by these means, underwent very remarkable improvement.

The Clinical Societies' Report gives no further suggestion as to treatment than is given above, except the removal of patients regularly to southern climates, during the winter.

Dr Mahomet, at a meeting of the Clinical Society of London on March 10<sup>th</sup> 1882<sup>(1)</sup>, related the successful treatment of a case of Myxoedema by administration of Nitro-Glycerine in doses of "<sup>1</sup>/<sub>50</sub> of a drop". Very rapid improvement ensued and in a fortnight after the commencement of treatment the swelling of the hands had greatly diminished - the patient could get on gloves which she had given up for years. Head-aches which had been constantly present were now gone completely and the skin was soft and moist. After two months treatment the skin was quite natural and in every particular there was a vast improvement.

One of the most remarkable instances of improvement under any treatment was in a case shown by Professor Grainger Stewart at a meeting of the Edinburgh Medico-Chirurgical Society, on December 7th 1887, and who at the time I write is in the Professor's Wards in the Infirmary undergoing the "Thyroid treatment".

Dr John Thomson, with whom I had some conversation about the case, and who had attended the patient after she left the hospital, told me that the patient was of an exceptionally active and energetic disposition which asserted itself in spite of the depressing effect of the disease, and this poor woman by her indomitable energy and perseverance accomplished for herself what almost amounted to a

(1) *Lancet*, March 18. 1882



cure for the time being. The case is of such interest in relation to the present subject and in showing what could be done even in an advanced case, if sufficient trouble were taken, that I feel I am justified in giving extracts from the account of the case which was published at the time."<sup>(1)</sup>

"The patient was married and aged 32.

She presented in a very typical manner the features of the disease. The treatment that had been tried for her in hospital was Iron, and Turkish baths. A certain amount of benefit seemed to follow the use of the baths; but as she had signs of mitral stenosis she was obliged to discontinue them. After leaving the Infirmary she hit on a method of treating herself which seemed to have been useful: - Rough towelling, brushes, etc., she did not consider hard enough for application to her skin, but a vegetable grater steadily applied by herself had been effectual . . . . .

Her progress had been steadily downhill since she left the Infirmary. In the middle of September 1887 she began the treatment the details of which were as follows: - On wakening in the morning she massaged the whole of her body most energetically for a considerable time, then rose and exercised all her joints systematically; next she sponged herself from the waist upwards with cold water, using a flesh brush till she felt warm. Then she did her household work. In the middle of the day she took a warm bath, using the flesh brushes again, and a vegetable grater till her skin was sore.

In the afternoon she walked for about two hours in the sun, trying to make herself perspire. In addition she improvised a hot air bath twice a week

(1) *Transactions of the Edinburgh Medical-Chirurgical Society* Vol. VII. page 50.

as follows : - She made as large a fire as possible in her small grate, took a warm bath before it (as on other days) then, in a thin nightdress, lay on a couch as near to the fire as possible and turned herself round till she began to perspire, this was usually in about an hour . She then drank cold water ~~water~~ to encourage the sweating, which, if she was not interrupted, usually went on for an hour or even two. Throughout the day she employed her spare moments in massage and moving her joints . . . .

Before treatment, there was very great swelling of her face, body and limbs, after it, in five weeks her face was so diminished in size as to be hardly recognisable, her clothes had to be taken in 8 inches at the waist and 3 at the neck, and her boots and gloves were much too big for her. Before treatment her movements were extremely slow and accompanied by severe pain. She was quite unable to stoop to clean her hearth but had to go down on her hands and knees to do so, and after had to crawl to a chair to help herself up. She could not knit, or sew, or peel potatoes. After treatment she was more active than most women, could go through any ordinary movements quickly, easily and without pain and could sew, etc., well. Before treatment she spoke with great slowness and much stammering, and ideas seemed to come very slowly. Her memory was extremely bad. After it she spoke rapidly and clearly and her memory seemed perfectly good."

I did not see the patient till she had been under treatment with thyroid extract for some time. She told me that she was not able to keep up the above treatment for many months after she had got into the greatly improved condition. Her heart

being weak and the exertion of massage, etc., being enormous, she relapsed now and then; but kept up a good deal of the bathing, scraping and rubbing constantly, till she came into hospital again for present treatment.

In the "Practitioner" for January 1893, Dr MacCall Anderson, of Glasgow, in a paper on "The treatment of Myxoedema," gives particulars of considerable improvement in a case of severe Myxoedema under the following treatment. - A mixture containing Strychnine and Arsenic was prescribed and she was shampooed daily for half-an-hour. Each day in rotation she had the following treatment : - First day, a vapour bath: second day, gr.  $\frac{1}{4}$  of pilocarpine subcutaneously: third day, a hot electric bath for half an hour. Each of these proceedings made her perspire freely. The roughness of the skin was very apparent during the shampooing, for the friction was audible at a considerable distance from the bed. Within ten days improvement was manifest. The skin became smooth and soft and felt almost natural. She felt warmer and the "shivering in the inside" and headaches completely disappeared. She began to menstruate freely, and the diaphoretic treatment was omitted for a week. The treatment was continued till she left hospital when the following notes were taken : - "The appetite is good - there is no headache - no coldness or shiverings, swelling of face, feet, etc., entirely gone, and the skin is soft and smooth. The movements are active and sprightly, she herself says, "she is an awful lot better". Dr MacCall Anderson recommends that similar treatment to this should be carried on simultaneously with the "Thyroid treatment."

Pilocarpine has been given with great success in



some cases, as for example in one case which I saw with Dr Melville Dunlop; this drug had been given by the late Dr Struthers of Leith, and the patient told me that before using it she had lived as if in a dense fog. All her senses were blunted; she seemed hardly able to originate a thought, and all impressions from without seemed to be partly lost before they reached her. When she had taken a few doses of Pilocarpine she seemed to spring all at once into a new existence and the fog to clear away.

## TREATMENT BY THYROID INJECTION AND FEEDING.

Thyroid Treatment.

The successful treatment of Myxoedema and Sporadic Cretinism by the administration of Thyroid juice was not arrived at by haphazard, as many successful cures have been; but by a process of reasoning which, considered merely from an intellectual point of view, cannot fail to arouse our admiration as a brilliant triumph of logical deduction.

I shall give here as briefly as possible, the successive steps of reasoning which Dr Murray employed in arriving at the remarkable conclusion which, being put to the test of experiment, resulted in the discovery of a cure for this, till now incurable, disease. It is always highly interesting to know how such discoveries are made, and luckily Dr Murray himself has given in a paper in the British Medical Journal, the following facts:- Myxoedema, of course, had, up till now, been thought an incurable disease; but since owing to recent researches, some light had been thrown upon the nature and probable causation of the disease, some hope had been entertained of permanently relieving the symptoms if not of curing the disease.

Professor Kocher of Berne noted that after

removal of the thyroid gland in man for goitre a set of symptoms always followed if the extirpation was complete, and these were afterwards shewn to be identical with those of myxoedema as we have seen above in the Clinical Societies Conclusions. Mr Victor Horsley's experiments with monkeys gave the same set of symptoms, so that there is no doubt that myxoedema is due to loss of function of the Thyroid Gland. Von Eiselsberg showed<sup>(1)</sup> that if the gland were successfully transplanted from the neck of an animal to some other part of the body, it was capable of continuing its functions, and thus preventing the onset of the symptoms which would have followed its extirpation; - Mr Horsley then suggested<sup>(2)</sup> that, as a means of arresting the progress of the disease, a healthy sheep's thyroid should be grafted into a myxoedematous patient.<sup>(3)</sup> This was successfully carried out, the grafted gland being placed beneath the skin of the infra-mammary region of the patient, and immediate improvement followed, and all the symptoms of myxoedema at once abated. Battincourt and Serrano of Lisbon, who successfully produced<sup>(4)</sup> this result, were of opinion that, as improvement commenced the day after the operation before the gland could possibly have taken on its functions as such in its new position, the improvement must thus have been due to absorption of the

(1) Schiff's experiments showed the same results } *British Med. Journal*, Feb. 8. 1890

(2) ----- }

(3) Bischer of Aarau had made same suggestion in 1839 } *British Med. Journal*  
+ had transplanted twice with temporary success i.e. till } July 26. 1890.  
absorption of transplanted gland.

(4) *British Medical Journal* Aug. 30. 1890. and Dr. Murray's paper.  
Kocher also had successfully transplanted in 1893



juice of the gland by the tissues of the patient. Dr Murray argued that to inject the juice of the gland hypodermically should naturally produce results equally good with the above; and considering that myxoedema was due to absence from the body of some substance which is normally present in the Thyroid gland, he thought that by restoring this substance artificially, he would be following quite rational treatment. He suggested this method of treating Myxoedema at the February meeting of the Northumberland and Durham Medical Society; and thereafter, as an opportunity offered itself in a well marked case of myxoedema, was able to put his ingenious theory into practice, with the result which now has become a matter of history. The following is the method of preparing the extract and of its administration, which Dr Murray has found to be the best, and which I give in his own words:- "The lobe of the Thyroid Gland of a sheep is removed as soon as possible after the animal has been killed. The surrounding fat and connective tissue are removed from it. All the instruments and glass vessels used in the further preparation of the extract should be either sterilized by heat or thoroughly cleansed with a 1 in 20 solution of carbolic acid. The gland is cut up on a glass dish into small pieces, and then placed in a test tube with 1 cubic centimetre of pure glycerine and 1

cubic centimetre of a 0.8 per cent solution of carbolic acid. The mouth of the tube is closed with a plug of cotton-wool, and the mixture allowed to stand in a cool place for 24 hours. The mixture is then placed in a fine handkerchief, which has previously been placed for a few minutes in boiling water. It is then firmly squeezed by screwing up the handkerchief so as to express as much liquid as possible through the handkerchief. By this means 3 cubic centimetres (50 minims) of a turbid pink liquid are obtained. This preparation which will keep quite fresh for at least a week, should be kept in a small bottle with a glass stopper. It is best to make the extract fresh each week, so as to avoid any risk of putrefaction taking place. This extract may be given in two equal injections of 1.5 cubic centimetres (25 minims) each during the week, so that at first the patient receives the extract of one lobe of a sheep's thyroid in the course of each week. After a time the injections need not be made so frequently. The injections are made with an ordinary hypodermic syringe, which is carefully washed out with a 1 in 20 solution of carbolic acid both before and after the injection is made. The surface of the skin is also carefully cleansed with the same carbolic solution, at the point where the injection is made. The loose skin of the back between the shoulder blades is a

convenient situation in which to make the injection". Dr Murray's case presented most of the typical symptoms and signs of myxoedema in a considerably marked degree, which it would be superfluous to enumerate here, as there was nothing extraordinary about them.

Treatment was begun in April 1891, and three months after this the patient was practically cured. The extract of two and a half whole glands had been injected all together. She had steadily improved since commencement of the treatment; the swelling had gradually passed off, leaving the skin loose, moist and soft. Expression had returned to the face - speech and general movements had become more easy and active; temperature had risen to normal; perspiration had returned freely and she had ceased to complain of feeling cold - menstruation also had returned normally, though she had not menstruated for four years. The mind became quite clear and active and in fact she had been restored "to her old self."

Dr Murray, in giving his discovery to the medical world, expressed a hope that others might be induced to give the treatment a fair trial, and it was not long before the Medical press gave publication to several other cases, successfully treated according to Dr Murray's method, by medical men in various parts of the kingdom namely, Dr Wallace Beatty of  
(1)  
Dublin, Dr Ernest Carter of the Lancashire County  
(2)

(1) *British Medical Journal* March 12. 1892, p. 544

(2) *Ibid.* April 16. 1892 p. 505.



Asylum and Dr Arthur Davies<sup>(1)</sup> of London.

It is a curious fact, that in the case of many discoveries, the same result has been arrived at by two absolutely independent investigators simultaneously. I believe it was so with the great theory of evolution, Darwin and Wallace coming to the same conclusions, in the main at least, practically simultaneously - so in this case, Dr Harry Fenwick seems to have been experimenting with Thyroid juice simultaneously with Dr Murray's experiments, and his conclusions were published in the same number of the British Medical Journal in which Dr Murray's paper appeared.<sup>(2)</sup> He had, however, come to the conclusion that myxoedema was due to perverted renal function, and that the improvement resulting from hypodermic injections of Thyroid juice was due to its diuretic action; though subsequent experiments by others have failed to corroborate this observation.

At the annual meeting of the British Medical Association held in Nottingham in July 1892,<sup>(3)</sup> the pathology and treatment of myxoedema were fully discussed and a number of medical men related the extraordinary success which had resulted from this method of treatment; and only one had negative results to give, namely, Dr Mitchell Clarke, who had been equally unsuccessful in both cases in which he had tried the remedy. Upon enquiry, however, I have learned that

(1) British Medical Journal - April 30. 1892. p. 911

(2) Ibid. Oct 10. 1891

(3) Ibid. Aug. 27. 1892

Dr Mitchell Clarke did not superintend the treatment himself; but left it, I think, to a house-physician in some hospital, so that he could not be sure that his cases received extract of thyroid at all.

The method of treatment by hypodermic injection of Thyroid juice, though practically universally successful, was nevertheless open to serious objection, and some very awkward ill-effects had followed, namely, the formation of abscesses at the seat of puncture and elsewhere, in spite of apparently the most scrupulous antiseptic measures; and in several cases alarming immediate effects, such as severe pains in different parts of the body, syncope, and, as in one of Dr Murray's own cases, loss of consciousness, tonic muscular spasms following the injection, probably due to the point of the needle entering a vein, an accident that can never be foreseen and is always liable to occur unless the injection be given exceedingly slowly. Again, as Dr Hector Mackenzie remarked in a paper from which I shall quote in detail immediately, "when it is remembered that those injections have to be personally administered for the remainder of the patient's life by the medical attendant, these risks, however, slight in regard to a single application they may appear, become immensely magnified when a long series has to be taken into account. These objections are of great moment as regards the future

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use of this plan of treatment, although not in the least detracting from the value and interest of the results which have so far been obtained."

By one of those curious coincidences which I have remarked upon already, these objections to the injection method seem to have presented themselves to three different medical men simultaneously, namely, to Dr Lundie of Edinburgh, Dr Fox of Plymouth, and Dr Hector Mackenzie of London, and the much more simple method of administering the Thyroid by the mouth seems to have occurred to each independently and subsequent trial of this method met with equally astonishing and successful results in cases treated by all these gentlemen, the results being in every way quite as perfect and satisfactory as those derived from the treatment by hypodermic injection.

Dr Fox, whose successful case was published in the same number, and side by side with that of Dr Hector Mackenzie in the British Medical Journal for 29th October 1892, began his treatment on June 2nd 1892, with a glycerine extract prepared by the patient herself, and his patient was directed to take the equivalent of  $\frac{1}{4}$  gland twice daily twice a week, at first, but afterwards was ordered to take half a Thyroid lightly fried and minced, with currant jelly



as well as the extract, the dose of the latter being greatly reduced. By mistake she took an overdose for some time, and the result was that she got rapidly weak, profuse perspiration breaking out on exertion, even when slight, and she could not walk or stand steadily. On the dose being properly reduced, she rapidly recovered ground and continued to improve till practically cured of myxoedema. Dr Hector Mackenzie administered the gland merely pounded, and occasionally as extract; but the quantities that he gave were enormous compared with what has since been found to be sufficient. He gave at a time two whole glands, and got consequently most marked and often unpleasant results such as high temperature - profuse sweating, nausea, aching pains, etc. Between August 9th and 16th she got 20 Thyroids by the mouth, ten of which were vomited. He recommends giving  $\frac{1}{2}$  a gland per diem, which will afterwards be seen is really almost a poisonous dose.

Dr Lundie's case, though treated at the same time as the last two, was not published till Jan<sup>y</sup> 14th 1893.<sup>(1)</sup> He began treatment by hypodermic injections on October 1891, but had to discontinue treatment after several months; for though he got satisfactory improvement, the patient suffered greatly from pains over the body, and a series of abscesses

(1) *British Medical Journal* for that date

which had arisen. After five weeks without treatment during which time the patient began to lose ground, Dr Lundie determined to give the extract by the mouth, which method was begun in July 1892, and proved as successful as the above cases. I saw the patient some days ago, at her home, by the kindness of Dr Lundie, and she struck me as having the appearance of as good health as a lady of her time of life can expect. She had a good fresh complexion and was well nourished and cheerful. She says that after the first 10 days or so of treatment, she seemed to be coming alive again after having been dead for years, and "she used to laugh to herself" for joy. She has sat all winter in her room without a fire, and is often quite warm when others are complaining of the cold. She is now keeping up small doses in the form of powders which are prepared by C.B.White, 20 High Road, Kilburn, London, N.W., and have the advantage of keeping for an indefinite period. Up to the present point, and in describing the above cases, I have intentionally avoided occupying space with details, and have not given at any length the particulars even of the progress of each case under treatment. My object so far has been merely to give a definite idea of the manner in which Dr Murray brought forward his method of treating Myxoedema, how it was eagerly taken up and

put to the test by medical men in various parts of the kingdom with practically uniform success; and how the treatment was finally immensely simplified, and still carried out in its perfected form with the same extraordinary success as attended upon the employment of the original form.

Acting under the belief that in such a paper as this the more important portions of the subject under consideration should, if possible, be given from the results of personal observation, I shall now give an account of a case which I have had the good fortune to have under my care, and which I have treated by the administration of Thyroid glands by the mouth. This has been in almost every particular a very typical case of Myxoedema, and the progress under treatment has been also very typical of the way in which the symptoms in that disease give way under the administration of the remedy: I shall therefore give it in considerable detail.

After this case has been given in detail I intend to give particulars more or less fully of several other cases of Myxoedema, and one of Sporadic Cretinism on which, though they have been under the care of other medical men, I have been enabled, through the kindness and courtesy of these gentlemen, to make personal observations, and several of which I have been able to watch under the whole course of



treatment.

In the position which I have held for about eighteen months of private assistant to Dr Burn Murdoch, I had frequently seen with him a case of Myxoedema of many years standing. When the first cases of "Thyroid feeding" had been published in the Medical journals, Dr Burn Murdoch, knowing the special interest that I took in the subject, most kindly permitted me to take the case in hand and the administration of portions of sheep's thyroids was commenced. The following are the particulars of the case noted according to the method of clinical investigation of a case of Myxoedema suggested in Dr Byrom Bramwell's "Atlas of Clinical Medicine."

1.



2.



Photographs of A.B. No 1. Taken a few days after treatment  
was begun. No. 2 about three months after.

## C A S E . I.

CASE OF A.B.      Preliminary facts.

The examination and taking of this case was commenced on January 12th 1893.

A.B., aged 46. Female. Has no occupation. In fact, she leads a sort of vegetable existence, sleeping, or lying dozing on a couch the whole day. She is married. Has lived in Edinburgh since, and she says for some years before the onset of symptoms, and in the same house for nearly all this time. She was born in Port Glasgow, which she left 27 years ago.

Complaints.

Great lassitude and disinclination for exertion; difficulty of speech, as if her tongue "would not work;" the same sort of feeling in the limbs, etc. as if the muscles "were bound;" unsteadiness in gait and inclination to fall; says she is always cold and has the greatest difficulty in getting up any warmth in the body, etc.

Family history.

This affords no information of interest except negatively. There has been no Goitre, Myxoedema or Grave's disease among her relations, no phthisis or



evidence of tubercle and no nervous affections.

Personal history.

A few months before the symptoms were first noticed, the patient had a particularly lingering labour. No special amount of anxiety or worry and no shock, etc. No great loss of blood at any time. Has had 8 children and no miscarriages, the last child died 16 months after birth, of 'inflammation of lungs.' No hereditary disease is manifested among the children. She has not been pregnant since this disease commenced.

History of present illness.

A.B. was originally a particularly active and cheerful woman, rather slightly made and of good general health with the exception of chronic disease of the bone of the left <sup>arm</sup> and right thumb, probably tubercular and which troubled her in childhood and early womanhood. In May 1886 she underwent a very lingering labour as above mentioned which was not abnormal in any other respect, however, and there was no excess of bleeding. This was the only troublesome labour she had experienced. She completely recovered from this; but 9 months later, i.e., in February 1887, she caught cold and a very severe illness set in, the exact nature of which cannot be made out; but there was a large amount of swelling all round the glands of the neck, and purulent catarrh

of the right ear with feverishness. She had fainting attacks on several occasions, and was extremely debilitated by the illness, so that she could not sit upright or lift her food to her mouth. She was "stone deaf" for some weeks. She is pretty sure that before this illness, she had been suffering from lassitude and a feeling of "laziness" for some time, but has no definite recollection of much being wrong. She was in bed for over a year with the above illness, and in the meantime, had become swollen up all over the body considerably; but she thought she was only getting uniformly fat. Then the face began to swell up, and every time she looked in the glass she saw that her looks had changed for the worse, the hair fell out and all the signs of Myxoedema developed gradually, till, about three years after the commencement, she was at her very worst, and continued so for about two years, and then commenced to improve; so that when I saw her first she was not nearly so bad as she had been.

Present condition.

As she presents very typically the characters of the disease I shall only mention any features that are in any way particular or specially marked.

Present condition January 13th 1893.

There is no capillary blush on nose or cheeks, but she says there was one spot about the size of a

shilling on the left malar region at one time. Eyebrows and lashes are almost completely absent, but the hair of the head is fairly plentiful. There are a good many of the characteristic scaly crusts among the roots of the hairs, and the hair of the head is very coarse and dry. There are fatty swellings of considerable size in the supra-clavicular regions. The thyroid gland cannot be felt. She is very sensitive to cold and is always wrapped up in thick shawls, etc. Hearing is somewhat impaired and speech very indistinct. She says her tongue "will not work" properly. Eyelids are very much swelled up and corrugator supercillii contracted. Her gait is very unsteady and she staggers from side to side, and has to hold on to tables and chairs, etc., as she walks. Complains of great weakness and lies down on sofa most of the day - memory is greatly impaired and ideas come slowly - no hallucinations, delusions, or tendency to insanity. She is not at all irritable, and Ord's expression "lethargic good temper" gives a good idea of her temperament. She is much annoyed by a great secretion of slimy mucous saliva flowing from her mouth, especially at night, and it soaks her pillow. Perspiration is quite absent. The ankles are generally swelled at night; but this disappears after a night's rest. Swelling of face and body is not nearly so great as it was two or three years ago.



She first noticed it about neck and face, and she says that her legs never swelled to anything like the extent of other parts, which were enormously enlarged. The eyelids and lips show the swelling at present very markedly, and the eyes have an extremely heavy, sleepy look.

Temperature 95.4° F. Pulse 80 & weak. Heart, etc., - Apex beat weak but regular - no bruit - apex beat is a little displaced down and to left side. Catamenia absent, though she has been "regular" till six months ago.

Urine normal: specific gravity 1015.

Bowels very regular - appetite poor, but digestion very fair.

The photograph No.1 - was taken unfortunately when treatment had been going on for a few days, and improvement had begun; but it shows many of the points in the physiognomy still, and is a considerable contrast to that taken three months later - No.2.

Commencement of treatment was delayed on account of the difficulty of getting the proper glands. Several butchers were applied to, but they had no idea that there was such a thing as a Thyroid in the sheep. I at last succeeded in getting a supply by going down to the slaughter-house, and enlisting the services of the inspector who has kindly supplied the patient with thyroids at intervals since.

T R E A T M E N T     A N D     P R O G R E S S .

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Treatment and Progress.

January 24th:  $\frac{1}{4}$  Thyroid ( $\frac{1}{2}$  a lobe) slightly fried and minced and taken with a little bread and butter: patient is not at all inclined to carry out the treatment, and smiles incredulously at the idea of any great improvement taking place.

26th: After taking her dose on the 24th, in the evening, patient noticed nothing until she was in bed, and she perspired during the night, the first time for seven years. To continue to take  $\frac{1}{4}$  gland every second day.

28th: Patient feels much more comfortable and warm, and begins to have faith in the remedy. Skin is certainly less rough and dry and harsh - pulse 80. Temperature 95.8°.

31st. After last dose patient perspired very heavily during the night. There is distinct improvement; movements are brisker, the swelling, especially about the eyes and lips, is less, speech more distinct, skin moist. Patient feels the treatment to be pretty severe upon her. She is carefully warned to avoid all exertion, and to lie down the most of the day.

Feb. 4th. Weight 11 st. 8 lbs. (unfortunately patient was not weighed before treatment was begun, for at that time she did not feel able to come for that purpose.) She now does not feel the remedy so hard upon her, and perspiration is not so profuse. Improvement goes on wonderfully.

8th. Is still having her  $\frac{1}{4}$  gland every second day. There is a most marked improvement already. She has let her supply of Thyroids run short, so has not had it to-day. Her hands are very noticeably smaller and more shapely; her wedding ring was, before her illness, so loose that it "used to fall off" as she says, and it has been deeply embedded in the surrounding oedema during the illness. It is thus a good index of the amount of oedema, and is now much less embedded. Pulse 86 - temperature 96.4° F. She is recommended to get a fresh supply of glands and to keep them in boracic acid.

16th. Weight 11st. 3 lbs. On the night of the 8th, patient suffered considerably after taking her  $\frac{1}{4}$  gland. She was nauseated, - an effect that the remedy has not had on her before. She was very restless, "dripping" with perspiration all night, and on the next day felt very weak and exhausted. However, she is now very enthusiastic about the "cure" and wishes to carry it out as effectually as possible in spite of present inconvenience ; so she took it



again on the 10th and was still much nauseated at the time of taking it, and could hardly swallow it all; but she did not vomit, and had not quite so bad a night. She is greatly pleased with the alteration in her appearance, and though she feels weak, she is otherwise much better.

21st. The disagreeable sensations after taking the doses have almost passed away. She still perspires considerably the night after taking it. I am inclined to think that when freshly got the thyroids are much more potent, and after keeping for a while they get hard, and possibly the juice soaks out into the boracic powder and weakens them. She has never had the severe pains in chest and limbs that have indicated an overdose in many other cases.

28th. Improvement goes on constantly; she is now looking "quite like her old self," as her husband says, though really there is still a good deal of oedema to be got rid of. There has been some desquamation, though no great flakes of skin as in some cases. The temperature has never gone above 96.8° yet, at least at the times I have taken it. There is no one in the house to whom I could safely entrust the taking of the temperature, so no satisfactory record of this can be made. Pulse is never beyond 88 when I see her. Her eyelids, lips, and ring finger are still losing their swelling. There has

been no appreciable increase of urine. Patient feels much more active, though not very strong. Her gait is better though still unsteady. Hearing is improved and speech is almost quite clear, and her tongue "works" better. The dandruff and scaly crusts among the hair have almost quite cleared away. The supra-clavicular swellings are not quite gone yet, though much less noticeable.

March 3rd. Patient now takes the gland substance raw and in a little jam; she has been going about the house and doing a little house-work, and is able to knit and sew easily and well, which were formerly out of the question. Yesterday and to-day she has been in bed, as she has begun to menstruate, the first time since treatment began and for six months before it. Advised to be very careful not to over-exert herself, and to rest on the sofa when she gets up again. Temperature 96.4°F: pulse 88.

11th. Weight 10st. 7 lbs. Improvement continues well still. She is now recommended to take  $\frac{1}{6}$  of a thyroid every day instead of  $\frac{1}{4}$  every other day as before. Temperature 96.6°F: pulse 90.

15th. Sent for me to-day, as she has been a good deal upset by the increase in the frequency and amount of dose. She was very sick and has vomited several times: she is much weakened and has been bothered with palpitation frequently. She is to re-

duce the amount by one half, i.e., to take  $\frac{1}{12}$  of a lobe each day.

28th. Had another, though less severe attack of faintness and vomiting, etc., on 23rd, and has taken no thyroid since till yesterday, when she took  $\frac{1}{12}$  gland. She is looking fagged, and has dark rings round her eyes. The heart is weak. The signs of Myxoedema, however, are rapidly disappearing still. Pulse 90. Temperature 96. I prescribed to-day a tonic containing Digitalis and Citrate of iron and Quinine. She is complaining of frequent loss of sleep, so I ordered her Sulphonal gr.xx every other night, and to discontinue the thyroids for a time.

April 5th. Weight 10st.  $1\frac{1}{2}$ lbs. Is looking much better and feels stronger. She is to go on with tonic, and still discontinue the thyroids.

14th. She has had no thyroid since 23rd March till yesterday, when she took  $\frac{1}{12}$  gland as she fancied that her eyes were getting swollen again. She got her wedding ring off for the first time since her illness began seven years ago. Has been taking short walks out of doors, and has got on splendidly. She is greatly astonished at her walking powers. She now feels "real strong" and the feeling of exhaustion and dark rings round the eyes are quite gone, and she has much more tone in her expression. She is to continue the tonic and to take  $\frac{1}{12}$  of a



thyroid every second day.

20th. Weight 10 st. 4 lbs. This is not due I think, to her having lost ground and become more myxoedematous; but the increase of  $3\frac{1}{2}$  lbs since the 5th is due to gain in flesh, for since that day she has undoubtedly been rapidly improving in health and strength, and looks in better condition generally; to continue  $\frac{1}{2}$  every other day and tonic.

26th. Patient considers herself cured, and says she has nothing to complain of in health, and thinks she could walk up Blackford Hill easily. She has taken several good walks lately, and has not been at all fatigued thereafter. Her appetite is very good. She sleeps better (without Sulphonal). She takes great delight in walking out to call on her friends who have only known her in her myxoedematous state. Her heart is practically normal now, and the pulse is firm and strong. She has not menstruated again since March 3rd, but as she is likely to be at the menopause, this is not to be wondered at. I hardly consider her to be free from the myxoedematous condition yet, however, and look for still greater improvement to come. She has still got the characteristic yellowish and slightly waxy look of the skin to a slight degree; but I have noticed this in all other cases which I have seen

that have been "cured" by this treatment, except Dr Lundie's case, and I think it is about the last symptom to pass away. In Dr Lundie's case, as that was the first treated in this part of the country, there has been more time for it to pass off. She had her photograph taken a few days ago, and it contrasts wonderfully with that taken three months ago. (See page 61.)

Such is my own particular case with its treatment and progress. Though the patient was Dr Burn Murdoch's, the fact that through his kindness, the case was entirely in my hands for treatment gives me some sort of right to consider it specially my case for purposes of treatment. I will now give in less detail some other cases which, though they were in the hands of others, I have, through the courtesy of those gentlemen who were attending them, been able to personally observe them, and thus the facts that I give about each, though gathered mostly from their notes on the cases, are partly the result of my own observation.

I will give first in order two cases which were and are still being treated in the Royal Edinburgh Asylum, and which, through the courtesy of Dr Clouston and Dr Elkins, who understood my interest in the subject, I have been enabled to watch from the time that treatment by "Thyroid feeding" was begun up to

the present time. These cases are good examples of Myxoedema with insanity and the insanity of Myxoedema, and also illustrate some other points that were not markedly shown in my case. For instance, I was unable to take sufficient observations of the temperature to form a chart in my case, whereas in the first of these cases, a beautifully typical chart is shown, and so on: I may therefore give these cases pretty fully.



## C A S E   I I .

## CASE   OF   C.D.

C.D.   aged 51.   Female, wife of a clergyman.  
Admitted to the Asylum in December 1892 - of good  
education.

Facts of Medical Certificates.   "She is suffering from insanity of Myxoedema with characteristic mental enfeeblement, suspicious of trifles and occasional loss of self-control with general apathy and mental hebetude."   Insanity had lasted under three years, she had threatened suicide, and was said to be dangerous "at times."

Previous history, etc. - extract from a letter received from the doctor in the asylum near her home, where she was at first placed.

He had seen the patient for the first time very excited and violent and using obscene language to her husband before the children. She said that her husband had been accused of murdering the children. She seemed to hate her husband, and applied to his Presbytery to have his conduct examined into and had assaulted him several times and expressed a desire for his death. She interrupted public worship on Sunday by a disturbance in the church, and frequently

used obscene and filthy language. After admission to that asylum, she soon settled down, and though her hatred for husband and children lasted some time, she gradually lost this feeling. She had curious notions as to causation of her state, i.e. that it was due to sexual causes, etc.

#### State on Admission to Edinburgh Royal Asylum.

State on Admission. - "Some exaltation." Is easy to please; pleasantly settles down in her new quarters; is facile; seems weak-minded; memory moderate; coherent, and can answer questions.

Appearance:- Typical facies of Myxoedema, bloated and heavy countenance, puffy eyes, deep pink cheeks, and hair grey and scanty; muscularity poor, considerable fatness. Lungs and heart apparently normal, but heart sounds are distant; tongue large, flabby, coated and indented.

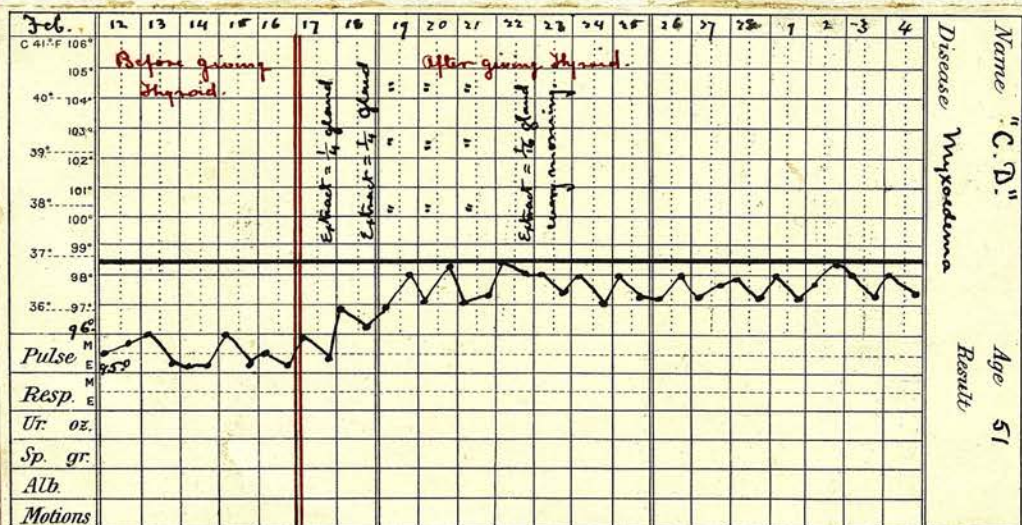
She is very pulpy, but the skin does not pit on pressure; it is very dry and parched. She complains of feeling cold, and likes a warm room. Her hands are short and stumpy and dry. Pulse 64, regular, poor tension. Temperature 97.6°F. Weight 14 st. 2 lbs.

#### Treatment.

The treatment was begun on 17th February. The



remedy was administered in the form of an extract made in the Asylum, each tablespoonful being equal to  $\frac{1}{16}$  of a gland, and she was given four tablespoonfuls daily for the first few days. Improvement commenced at once as far as her physical condition went. The temperature, which was 95.4° before the first dose, went up to 97° the day after, up to 98° the following day, and continued more or less at about 98°. (See chart below).



The face soon began to show more expression, (or rather some expression), and the hands, etc., to get thinner and more natural in shape. Patient said she felt lighter and comfortably warm. Hot baths were given frequently. The effect on the mind was not satisfactory at first. Dr Elkins' note about this was "The medicine (thyroid) certainly seems to make her temporarily worse mentally, more suspicious



unreasonable and querulous. One day she refused the medicine absolutely, and she cannot be persuaded to take a tonic." It was thought that a stomachic and tonic would do good, as the tongue was coated with dirty white fur and she had no appetite and the pulse was feeble. In this case the thyroid extract showed a very distinct irritant effect on the stomach nauseating patient and causing attacks of vomiting occasionally, and one morning she nearly fainted in her bath. On this account the dose was reduced to  $3\frac{1}{2}$  (16 gland) every morning, and this became her regular daily amount; but even this upset her now and then, so the treatment had to be suspended for a day or two at such times. She was ordered  $\frac{1}{2}$  pint of champagne daily, and took drives and short walks. It was curious to observe how tanned the old dry skin, which had not yet been thrown off became on her face from exposure to the sun; so much so that she said "It was dreadful, and she was becoming a nigger." The signs of Myxoedema very rapidly disappeared, and her stomach improved. She had lost a good deal of hair during the illness; but now it grew in in the most astonishing manner. At last her mental symptoms showed signs of definite improvement also, and on 20th April, the day on which I saw her last, the nurse told me that one could hardly notice

that she was insane; she was pleasant in manner, had lost her querulousness and suspicions, etc., and the great pleasure she derived from a letter which she lately got from her husband showed how the old animosity must have passed away. In fact, both in mind and body she is immensely improved and transformed. She now gets 3 ~~4~~ of the extract thrice weekly. Her weight is now 12 st. 1 lb., and thus she has lost 2 st. 1 lb. under the thyroid treatment.

## C A S E   I I I.

CASE OF E.F.

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E.F. aged 50; married; a housewife.

The present is the second time she has been in the Asylum as a patient. She seems to have been affected mentally for about three years; but how long the symptoms of Myxoedema have been present is uncertain. The cause of her insanity is said to have been "taking too much port-wine medicinally, and too much brandy surreptitiously." But it is probable that Myxoedema existing before, the alcohol was sufficient to overturn the already unstable mental equilibrium.

She evidently had all the symptoms of Myxoedema when admitted on the first occasion in October 1891, and she was excited, delusioned and full of suspicion. After being in the Asylum for a fortnight on careful dieting, but no other special treatment, that is noted, she was discharged greatly improved mentally, and apparently physically also.

She was admitted again on 20th December 1892, in much the same condition as at first, only more aggravated, with very pronounced delusions and



suspicion, thinking that her relatives were all persecuting and injuring her, and that electric batteries, gas engines, etc. played under her bed all night, and was also so violent that the police had to interfere. The symptoms of Myxoedema were exceedingly marked, and she was swollen up to an enormous degree.

Treatment was begun on February 18th, 1893, with the same extract as was used in the case of C.D., and the same quantity to begin with, i.e. -  $\frac{1}{4}$  gland. This was, however, found to be too much, and  $\frac{1}{8}$  was given every morning. Improvement both in mind and body went on uninterruptedly from the first except for occasional pains in the body and joints, vomiting, sick feelings and headaches, which were never persistent, and were relieved by stopping the treatment for a day or so.

On April 6th the following note was made:- "It would be impossible now to diagnose Myxoedema from her appearance. She is still at times a little querulous, but hardly ever unreasonable as she used to be. She is much more cheerful and energetic. Small hairs are appearing on the vertex."

The temperature chart is not quite so typical as that of the last case, but is given below :-



The following are some measurements taken at the commencement of treatment and when improvement had become well established:-

	February 19th	April 7th.
Abdomen.	49 inches	43 inches
Bust.	48 "	40 "
Arm.	13 $\frac{1}{2}$ "	12 "
Wrist.	8 $\frac{1}{2}$ "	7 $\frac{1}{2}$ "
Calf of leg.	15 "	14 $\frac{1}{2}$ "
Ankle.	10 "	10 "
Weight on February 19th.	April 7th.	

The following two cases, besides being additional examples of the efficacy of "thyroid feeding," illustrate in a very extraordinary manner the heredity of Myxoedema. The patients are twin sisters, one having suffered from the disease in a very marked degree for twelve years, and the other, after nursing her during seven years, to her extreme horror developed the same symptoms and suffered from them for five years. Dr Melville Dunlop who has known these ladies for many years, and has most kindly furnished me with every opportunity of becoming acquainted with their cases, says that he has not the slightest hesitation in saying that another sister, who died seventeen years ago and whom he remembers well, was a very typical and far advanced case of Myxoedema. About their mother, I may quote from his notes as



follows:- "The following is an extract from a letter written by their mother in 1849, three years after their (the twins) birth, she herself being at that time about 40 years of age - "I am getting very old-like, and have much difficulty in getting about. My colour is very bad and I am exceedingly stout without being strong; I am assuming the corpulent look of advancing years to my great dismay." A bust of this lady, the cast for which was taken after death, bears many of the characteristic features of Myxoedema - especially noticeable in the thickened lips and the swelling under the eyes. Her nephew, now a well-known Scottish Academician, says that from his remembrance of his aunt he has not the least doubt that she suffered from Myxoedema, and other relatives bear him out in this opinion. Dr Melville Dunlop has been treating these two ladies with thyroid extract by the mouth with great success. He has also had four other cases of Myxoedema under this treatment; and as he has most courteously given me opportunities of visiting the patients in their homes, and has given me his notes on all these cases, and kindly permitted me to make free use of them, I am enabled to give here such of them as are of special interest. I will, however, confine myself to the cases of the twin sisters, for the others, though very valuable as additional examples of the success of

the treatment, have nothing in them of sufficient special interest to make it worth while giving them in detail here. I believe, however, that all Dr Dunlop's cases are to appear in detail in the forthcoming number of the Edinburgh Medical Journal, which is to be specially devoted to the subject of Myxodema.

## C A S E    I V .

CASE OF G.H.

G.H., aged ~~about~~ 46 - spinster.

This patient had all the common signs and symptoms of Myxoedema. She was of enormous size, and could not move about or use her hands or arms in any useful action for the last 7 or 8 years. She became exhausted on the least exertion and suffered from frequent syncope. She also suffered from constant cramps and pains in the muscles of the back and limbs. Her skin was very dry and scaly - she had numerous small warts on the neck, and patches of brown pigmentation. She accepted her illness philosophically, however, though her mind wandered a good deal and she was very forgetful. During the few months preceding treatment she had been much worse mentally and physically, and had been confined to bed entirely. She had gradually become quite childish and had hallucinations of sight, smell and hearing. She continually declared that people in the next house annoyed her by speaking along electric wires connected with her bedroom. She saw people whispering about her, and complained that all sorts of animals annoyed her by their peculiar sounds. Mental symptoms became worse, and patient became sleepless



and restless and refused food. Acute mania developed, she threw things about the room, called out loudly continually, and wore a wild and anxious expression. Her excitement was so great that it needed great strength to keep her restrained. She had been thus for over six weeks and under mental nurses, when the thyroid treatment was determined on by Dr Dunlop with faint hope of success.

Treatment - October 18th 1892 - 20 drops of Brady & Martin's thyroid extract given thrice weekly.

By 30th October excitement quite gone and patient was resting and sleeping quietly. Had no longer any hallucinations and spoke naturally and eat freely. Very weak, however.

November 12th. Feels as if recovering from a long and severe illness, and remembers only having been in a peculiar and excited state. Temperature 98.8° F. Face smaller and more mobile and speech freer - feels warmer and comfortable, perspires slightly, and bowels move now regularly without medicine. Dose of thyroid extract reduced to minims 20 twice a week.

November 24th. Improving still - speaks naturally. Has severe aching pains over limbs and upper part of chest and neck.

December 7th. Skin soft and satiny - muscles no longer hard and boardlike to feel. Pulse can be felt at wrist. Sang an old English ballad right

through without effort.

December 28th. Body about  $\frac{1}{2}$  its former size and face much smaller. Complexion clear and natural and the brown patches on skin gone. Since her illness began she developed a bald patch which existed for many years but now the hair is growing in quickly and thickly.

January 14th. Patient now able to be out of bed and to sit up and can now knit and sew beautifully. The extract now given only every second week. Her abdomen has lost in girth 4 inches, waist 5; calf  $3\frac{1}{2}$ , upper arm  $1\frac{1}{2}$ , fore arm  $1\frac{1}{2}$ .

February 1st. Temperature has been at normal since 10 days after treatment was begun. Two months ago her weight was 14 st. 10 lbs., now it is 10st. 9lbs. There were no bad results from stopping dose last week. I saw the patient on the 12th April. The slight yellowish and waxy colour of the face was really the only thing that could possibly suggest Myxoedema. She talked a great deal in a rapid and lively manner, and seemed very happy about the wonderful change in her life. She was crocheting dexterously as she conversed, and appeared to me to be an intelligent sensible lady in remarkably good health.

## C A S E V.

CASE OF J.K.

J.K., aged 46, twin sister of the case G.H. The onset of her illness was very gradual. She began to feel easily tired and disinclined for any exertion, and thought it was only laziness and would wear off. She began, however, to suffer from stiffness and cramps in the muscles and difficulty in rising from a chair, etc. Her speech became slow and thick. She felt the cold very severely. She became irritable and very melancholy, for having nursed her sister and observed her miserable state, she was able to realise what she must inevitably come to, and it affected her deeply, and she told me that the thought of her fate used almost to render her insane. She gained about 2 stones during her illness, which lasted five years, and her temperature was usually about 96°.

Treatment - October 8th 1892 - 20 drops of Brady & Martin's extract was given thrice a week and she was warned not to exert herself in any way and to stay in bed the day on which she took the dose.

October 18th. Feels warm and comfortable. Temperature normal. Speech less deliberate. Swelling distinctly less.



October 28th. Speaks quite fluently and naturally. She suffers no more from mental depression. Skin soft and flexible.

November 8th. Has lost 10lbs. weight - former shape and expression of face is restored. She has lately had a good deal of aching pain in chest, abdomen and limbs.

November 20th. Can play on piano, knit and sew with ease, and is gaining strength constantly. She has been troubled with palpitation of heart and the pulse is irregular and intermittent - dose is reduced to 20 drops twice weekly - given a tonic and advised to keep bed for a few days. X

December 2nd. Palpitation, etc., less frequent - dose still further reduced, however - 15 drops twice weekly.

December 16th. General appearance - speech and temperament are virtually the same as before her illness.

January 10th. Feels quite well and says she is cured. She is as active as ever. Hair growing in well. Dose now only 15 drops once a week.

January 18th. Has lost over 2 stones weight and the measurements all over body are much reduced. Dose still further reduced to 15 drops every other week.

February 1st. There has been no loss of ground owing to the diminution of dose.

I saw her also on the 12th April and had I not

known of her previous history, I could never have had a suspicion of Myxoedema. She is an active slightly made little body and very talkative. She can now take good long walks and feel no fatigue after it - during her illness if she could get the length of the third lamp-post from her door she was well pleased.

The last case of Myxoedema that I propose to give the particulars of, is one which illustrates the dark side of the subject of treatment by Thyroid juice and emphasises in a very marked way the dangers which exist under the use of this powerful remedy.

## C A S E VI.

CASE OF L.M.

L.M., female. This patient had been under the care of Dr John Thomson, by whose kindness I am enabled to give the following particulars:- Since 1887. She had all the ordinary signs of Myxoedema which had been to a certain extent relieved by taking 30 minims of Tinct. Jaborandi thrice daily and this kept her skin comfortably moist. But during the last few years she had ceased to require it and had had no special treatment. She had always been complaining of great weakness and lassitude; but four months previous to commencement of thyroid treatment, she had suffered very much pain, angina pectoris, but it passed off and only recurred at long intervals. The present condition, i.e., at commencement of treatment is worse than her condition has ever been with regard to the Myxoedematous symptoms.

Treatment. Patient was ordered  $\frac{1}{4}$  sheep's thyroid twice a week.

31 December 1892. She has had three doses of the thyroid. She complains of slight headache: but no other effects have been noticed. To take  $\frac{1}{2}$  thyroid, twice a week.



6 January 1893. The patient has been complaining of severe angina pectoris. It comes on chiefly after exertion. On enquiry it is found that L.M. has been exerting herself more than usual, her servant having gone for a holiday. The heart sounds are weak but otherwise quite normal. The swelling of the face is much less. Nitroglycerine (m.i. of the 1 % solution) ordered every 4 hours.

12 January. She feels a little better, the nitroglycerine relieves the pain considerably. She is very weak. Ordered to stop thyroid and to stay in bed. She has had in all  $2\frac{1}{4}$  thyroids, the last dose being on January 10th.

\*

17th Jan. Still very weak; swelling of face almost quite gone; sweating profusely, no appetite, great nausea, tongue much furred, much pain over stomach, the heart pain scarcely felt, etc.: pulse 110, temperature 98.6 . Nitro-glycerine only to be given if heart pain is very bad.

23rd Jan. Got up and nearly fainted. Pain in stomach severe; constant nausea but no vomiting. Pulse 108, very feeble, but quite regular. Ordered hydrochloric acid and pepsine.

24th Jan. About the same. Ordered not to sit up at all, and to have nothing but peptonised milk and whisky every three hours.

26th Jan. Pulse and tongue both better; ordered Tincture of Digitalis m.X thrice daily.

27th Jan. 4.30 p.m. Pulse if anything stronger and tongue cleaner. Feels about the same.

9.30 p.m. Sat up to get her bed made; fainted and died.

Post-mortem Examination.

Cerebral arteries atheromatous; Pituitary body enlarged and very firm, size of a small bean; its fossa much too deep.

Thyroid body: both lobes about normal in outline, but extremely flabby and thin (like collapsed bladders) so that they could scarcely be felt among the other tissues.

No remains of Thymus.

Heart, etc. Slight thickening of mitral valve; otherwise all valves are normal; muscular tissue of wall of heart in a state of extreme degeneration; in places it seems to be replaced by fibrous tissue and in other parts almost completely by fat, owing to atheromatous changes having obstructed coronary arteries; numerous atheromatous patches in first part of aorta.

I have given this case with its progress and finally post-mortem, at greater length than it, at first sight, would seem to merit. But the very distinct and complete way in which it illustrates the great, and I believe only, danger<sup>to life</sup> of this treatment is I think sufficient excuse. Dr Thomson says about this case that death was of course due to the state of the heart, but that it was still impossible to say that it was not hastened by the thyroid treatment. When we note the condition of the heart in this case, and remember that in a great many cases of Myxoedema the heart is weak and dilated, (some observers say in all cases), the lesson we should learn is:- that where there is any reason to suspect cardiac weakness, even when no bruit is heard, (there was no bruit in this case), to warn the patient most carefully against all exertion and if necessary to



confine her to bed for the first few weeks of treatment.

The following case of sporadic cretinism treated by thyroid feeding is also one of Dr John Thomson's. It is to appear in the forthcoming number of the Edinburgh Medical Journal; but he has very kindly permitted me to give it here as it is the case from which I have derived most of my personal experience of the disease, though I have also been able to observe another case of his and several others, including a most curious case of Dr Bramwell's.

1.



2.



Photographs of Case of Spasmodic Tetanus "N.O." no. 1. Taken before treatment.  
no. 2. when treatment was well advanced.

## C A S E   V I I .

CASE OF N.O.  
SPORADIC CRETINISM.

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N.O. aged 18 years and 8 months.

There is no history of any of the "thyroid" diseases in the family, and except for temporary mental affection in a maternal uncle, no nervous or mental or tubercular disease in the family. Parents strong and well-grown. Patient was not much more backward than most children until his second year, when the parents noticed he was not growing. His teeth were not late. Not until he was six years of age did the parents realise thoroughly that he was more than merely backward in development. During the last fourteen years, he has grown little if at all in height, although he has got broader and stouter. His mental condition has gone back in that time, so that he is said to be much less intelligent than he was at five years old.

State on Examination (December 1892).

The patient is  $33\frac{1}{2}$  inches in height, and presents the typical ungainly appearance of a sporadic cretin. The head is  $20\frac{1}{8}$  inches in circumference. The fontanelles are closed. The hair is dark brown,



coarse and scanty. Complexion is that characteristic of Myxoedema, pale yellowish and waxy looking. The eyelids are swollen and puffy. The nose is thick and somewhat turned up. The lips big, thick and pale; the ears are well-formed.

The teeth are all of the temporary set; the second dentition not having begun; many are decayed and ground down. The tongue is big although it does not protrude.

The neck is very thick, so that it appears short, and on each side of it there is a large flat fatty tumour in the posterior triangle. There are smaller swellings of a similar nature in front of each axilla, but none in the back of the chest. The rings of the trachea can be felt pretty distinctly and nothing can be made out in the position of the thyroid.

The thorax is natural in shape, and the heart normal. Abdomen prominent, and a small umbilical hernia is present. There is slight dorso-lumbar lordosis. The limbs are short and thick, the hands and feet broad and comparatively large. There is slight outward bowing of the leg-bones.

The skin all over the body is dry, harsh and scaly. Large flakes of skin come off on to his clothes. There is considerable swelling of the sub-cutaneous tissue everywhere. There is no hair on the

face, pubes or axillae. Numerous small moles in various situations. The genital organs are small and infantile in form. Temperature is always sub-normal. Patient is very chilly, and always likes to sit close to the fire. Nervous system:- cutaneous sensibility dulled. Bowels regular; micturition also regular. Knee-jerks well-marked.

Intelligence is like that of a child of 3 years old. He can repeat one or two verses of hymns; can name the numbers up to ten, but cannot count objects. His voice and laugh are loud, cracked and un-childlike. His enunciation is indistinct and deliberate. Very fond of music, and can sing in tune after a fashion. He notices a good deal more than one would imagine.

If left to himself, he sits apart and becomes torpid, and would sleep all day if he were left alone, but brightens up when attention is paid to him. Specially drowsy in cold weather. Irritable at times. Very much attached to his doll. His memory is pretty good. He recognised at once a sister who had been absent for five years.

Treatment. He was ordered  $\frac{1}{4}$  of a sheep's thyroid by the mouth twice a week.

Jan. 1st. After his dose he suffers from headache and pains over the body, sleeplessness and rest-

lessness at night.

Jan. 11th. Pains, etc., continue, but face and body are distinctly less swollen. To have  $\frac{1}{8}$  gland twice a week.

Jan. 14th. Pulse 140; temperature  $98.8^{\circ}$  Swelling still less, and skin much softer. As ill effects continue, the treatment is stopped meantime.

Jan. 24th. Feels much better. Pulse 110; temperature  $98.5^{\circ}$ . Great improvement in appearance, and his demeanour and complexion much more child-like. The supra-clavicular and other fatty swellings have disappeared. Speech clearer. To resume  $\frac{1}{8}$  gland twice a week.

Feb. 25th. During last month he has rapidly improved in almost every way. He has grown two inches in height, measuring now  $35\frac{1}{2}$  inches. Mentally he is much brighter. Rate of growth considered a danger, and he is to have now only  $\frac{7}{8}$  gland twice a week..

March 22nd. Has been exceedingly bright and well since last note, and his appearance has wonderfully improved. Has not grown, however, during last three weeks; this apparent arrest of the former rapid growth is probably mainly owing to the very considerable bending of legs. Recommended cod-liver oil.



April 1st. Has been kept off his feet a good deal, and has grown an inch since last note. The two lower anterior molars are being pushed right out apparently by the approach of the second set of teeth.

12th April. He now measures fully 36 inches, and general improvement continues.

The photographs given below, and which I have had printed from plates kindly lent to me by Dr. Thomson for the purpose, illustrate very well the improvement in the patient's appearance which has taken place.

The above cases illustrate in the most wonderful manner the extraordinary therapeutic value of the discovery made by Dr Murray, in giving us what may almost be called a cure for Myxoedema and Sporadic Cretinism. I have spoken of it as a cure throughout this paper; but no doubt as the diseases are never, so far as has been shown, completely got rid of though kept so much out of sight by its occasional use as to be practically so, it is not strictly speaking a cure. It seems not at all unlikely that the new field of therapeutics opened up by this discovery may be still further extended, and other little-understood diseases may perhaps now be as successfully treated by extracts of other organs, glands, etc. One of the very first thoughts that crossed my mind on reading Dr M's paper, was the possibility of such treatment. At the meeting of the Medical Chirurgical Society of Edinburgh, on February 15th and 16th (mentioned above), at which Myxoedema and its new treatment were discussed, Dr Affleck remarked on the possibility of Dr Murray's discovery leading to analagous treatment of other diseases, and suggested the trial of an extract of suprarenal capsules for the cure of Addison's disease. Some work in the same direction has already been done, as I see from the medical papers,<sup>(1)</sup> where it is said that some pioneers of therapeutics have been giving raw

(1) *British Medical Journal* Jan. 14. 1893  
*Ibid.* - March 4. 1893. p. 452

pancreas by the mouth with beneficial results in diabetes mellitus. However, Dr Neville Wood from observations of 2 cases treated in this way with improvement, says he has little hope that diabetes can be influenced by pancreatic *preparations* in same way as Myxoedema is by Thyroid juice.

But the most astonishing results from treatment by such therapeutic agents have just been published by Dr Charles Macalister of Liverpool, who in a highly interesting paper in the B.M.J. for April 8th 1893 has just forwarded a very ingenious theory, that just as Thyroid juice, - as he says, - seems to exercise an inhibitory influence on the growth of mucous tissue, the predecessor of ordinary connective tissue, - and its absence therefore favours the growth of this tissue and produces Myxoedema, so also the secretion of the Thymus may have an inhibitory influence on the growth of muscle fibre, and its premature loss of function may produce pseudo-hypertrophic paralysis. He has apparently, by the exhibition of Thymus glands, caused a wonderful improvement in a case of this disease, and acting on an analogous theory concerning Lymphadenoma has produced marked benefit by the administration in such a case of a preparation of bone marrow, and he thinks it "not impossible that the application of this principle may ultimately lead us to treat some local overgrowths



of tissues either embryonic or more fully formed, such as sarcoma and carcinoma by the introduction into the system, of materials which may inhibit their production." Again, Dr Byrom Bramwell has been subjecting a case of acromegaly to treatment by ingestion of extract of the pituitary body, but the result has not been published. At the above mentioned meeting of the Edinburgh Medico-Chirurgical Society, Dr Byrom Bramwell exhibited a case of very acute psoriasis upon which the thyroid treatment had been tried with most extraordinary success, the scales which had been very numerous and thickly accumulated, were rapidly thrown off leaving a beautifully healthy skin behind. The remarkable desquamation in one of his cases under the treatment had suggested its use in this case. Here again is another field of therapeutic possibility opened up. How many cases of persistent psoriasis, eczema and ichthyosis might not be benefited by it?

What is the best preparation or form of this wonderful remedy to administer? and what is the proper dose? are questions which are constantly asked. I think to a great extent the answer to these questions depends upon the individual patient. For a patient in good circumstances, I think the powder is no doubt the best preparation for it keeps for an indefinite period; but as the raw glands can be got

so far at very little expense, if any; though no doubt, when the butchers awake to their value, they will cost their weight in gold, for poor people they are best and really very easily taken. The variety of doses that have been given is surprising. Dr Hector Mackenzie gave 2 thyroids daily - others give  $\frac{1}{16}$  twice a week and so on. The method of giving a gland or a certain part of a gland as representing a definite amount of thyroid substance is manifestly fallacious, the weight of different specimens being so widely different, though few seem to have realised this, and I believe that Professor Fraser is the only one who has prescribed the thyroid substance by weight. It seems that the average weight of a lobe of a gland is 60 to 70 grains, and in Professor Fraser's <sup>a</sup> words a sufficient dose by weight was always given to keep the temperature up to normal or just above it.

<del>This was found to be,</del>			
<del>1st month</del>	<del>30 grains</del>	<del>twice a week</del>	
<del>2nd "</del>	<del>40 "</del>	<del>thrice "</del>	
<del>3rd "</del>	<del>60 "</del>	<del>" "</del>	

~~the reaction being much less marked as time went on.~~

In what Dr Murray calls the second stage of treatment, i.e., after the patient's normal condition is reached, and has only to be kept up by occasional doses, of course the suitable dose for each

individual must be discovered by experiment.

It would form a very fitting conclusion to such a paper as the present, if one could give only a short account of the physiological action of the Thyroid juice - our knowledge on this subject, however, is very limited.- We know that it has some very powerful action upon the skin and its appendages for we cannot but notice how under its use a rejuvenescence of the skin takes place, the old atrophic skin being thrown off, sometimes in great flaps as from the feet of a case of Dr Bramwell's, and a soft satiny new growth of skin comes up in its place. The hair springs at once into rapid growth and the bald become hairy - the rapidity of growth which may take place being beautifully seen in a case at present in Dr Bramwell's ward in the Infirmary - where the hair not being able to get loose of the old cuticle fast enough coils up under it in a little spiral, till the force of its growth lifts off the obstruction. The nails also take on new growth, and it is interesting to note the sharp line of demarcation which marks off the old brittle and furrowed part of the nail from the new and smooth portion. The teeth in Sporadic Cretins show a like growth, the old worn representatives of the primary set being jostled out of their sockets by the vigorous growth of the second set.



The sweat glands take on vigorous action and perspiration occurs freely.

The marked actions of the thyroid juice on the body heat, not sufficiently accounted for by the increased perspiration, I think, is also remarkable. The general metabolism and growth of the body are actively stimulated; and in fact the body itself, with all its functions, is brought as near to the normal standard as antagonistic influence will allow.